The Radical Cyclization Approach to Morphine. Models for Highly Oxygenated Ring-III Synthons

Kathlyn A. Parker*,[1] and Demosthenes Fokas

Department of Chemistry, Brown University, Providence, Rhode Island 02912

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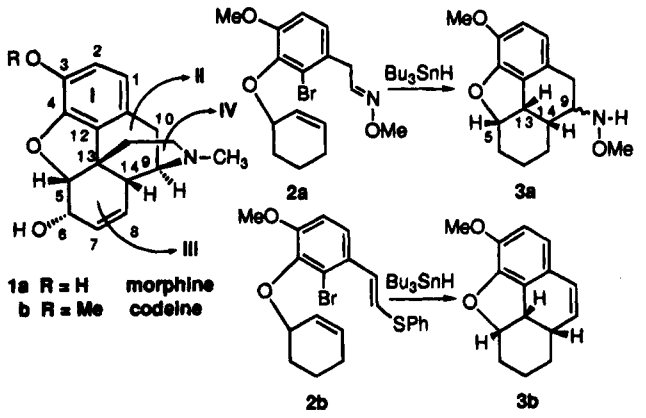
4-Iodo-3-methyl-2-cyclohexenone (**9**) and 3-alkyl 3-cyclohexene-1,2-diol derivatives **16** were examined as ring-III equivalents for the tandem radical cyclization approach to the synthesis of morphine (**1a**).

Introduction

A tandem cyclization initiated by an aryl radical has shown considerable promise as the key step in a projected synthesis of the morphine alkaloids (**1**).[2] By this method, the easily attainable *O*-methyloxime **2a** was converted to a pair of stereoisomers **3a**[3] and enol thioether **2b** was converted to a single product **3b**.[4]

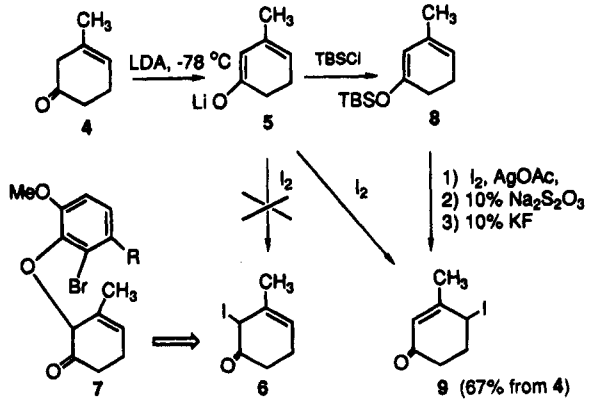


In order to apply this approach to the total synthesis of morphine, we needed to establish its viability with more elaborate substrates, specifically those in which the cyclohexenyl ring carried a functionalized two-carbon chain at the latent C-13, which might eventually become the ring-IV bridge, and at least one additional functional group, which could be parlayed into the C-6, -7, -8 allylic alcohol system. Anticipating that the greater difficulties would be encountered in the preparation and utilization of more highly oxidized ring-III synthons, we decided to confront this chemistry directly. At the same time, we were able to incorporate a C-13 substituent into the model structures. For convenience, a methyl group was used in preliminary studies and later a functionalized ethyl group was introduced.

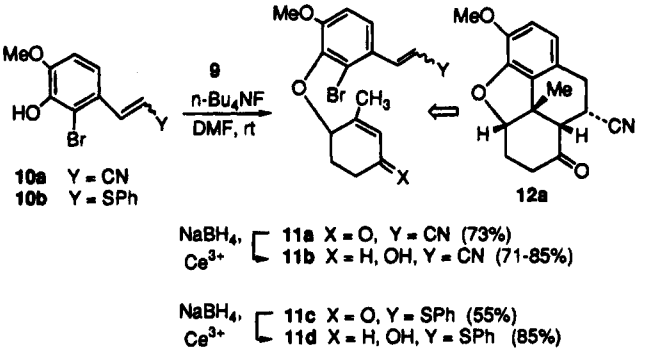
Results: Choosing a Ring-III Equivalent

Initially we hoped to prepare appropriate cyclization substrates of general structure **7** (Scheme 1) by alkylation

Scheme 1. Synthesis of 4-Iodocyclohexenone 9



Scheme 2. Synthesis of Substrates from 4-Iodocyclohexenone 9



of a halogenated phenol with a 2-halo-3-cyclohexenone (e.g., **6**). We postulated that an α-halo ketone of this type might be obtained by halogenation of the enolate of a 3-substituted cyclohex-2-enone (e.g., **5**[5] from **4**). Contrary to our expectations, iodination of enolate **5** afforded the 4-iodo-2-cyclohexenone **9**.[6] Likewise (as expected), iodination of the silyl ether **8**, derived from this enolate, gave enone **9**.[7]

Without access to the desired α-iodo ketone **6**, we modified our strategy to take advantage of the readily available γ-iodo enone **9**. If aryl ethers **11** (Scheme 2) derived from **9** would undergo tandem cyclization, the resulting tetracyclic compounds (e.g., **12a**) might be manipulated to afford compounds with the morphine

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(1) Recipient of an NSF Career Advancement Award, 1992–1993.

(2) For a preliminary report of the successful conclusion of these efforts, see: Parker, K. A.; Fokas, D. *J. Am. Chem. Soc.* **1992**, *114*, 9688.

(3) Parker, K. A.; Spero, D. M.; Van Epp, J. *J. Org. Chem.* **1988**, *53*, 4628.

(4) Parker, K. A.; Fokas, D. *J. Org. Chem.*, previous paper in this issue.

(5) Rubottom, G. M.; Mott, R. C. *J. Org. Chem.* **1979**, *44*, 1731.

(6) Similarly, quenching enolate **5** with bromine (1 equiv, CH_2Cl_2) at −78 °C gave 4-bromo-3-methyl-2-cyclohexenone.

(7) 4-Halo-2-cyclohexenones have been reported previously. For example, 4-bromoisophorone (4-bromo-3,5,5-trimethyl-2-cyclohexenone) has been prepared by treating isophorone with *N*-bromosuccinimide. See: Marx, J. N.; Carnrick, A. W.; Cox, J. H. *J. Org. Chem.* **1972**, *37*, 2308.

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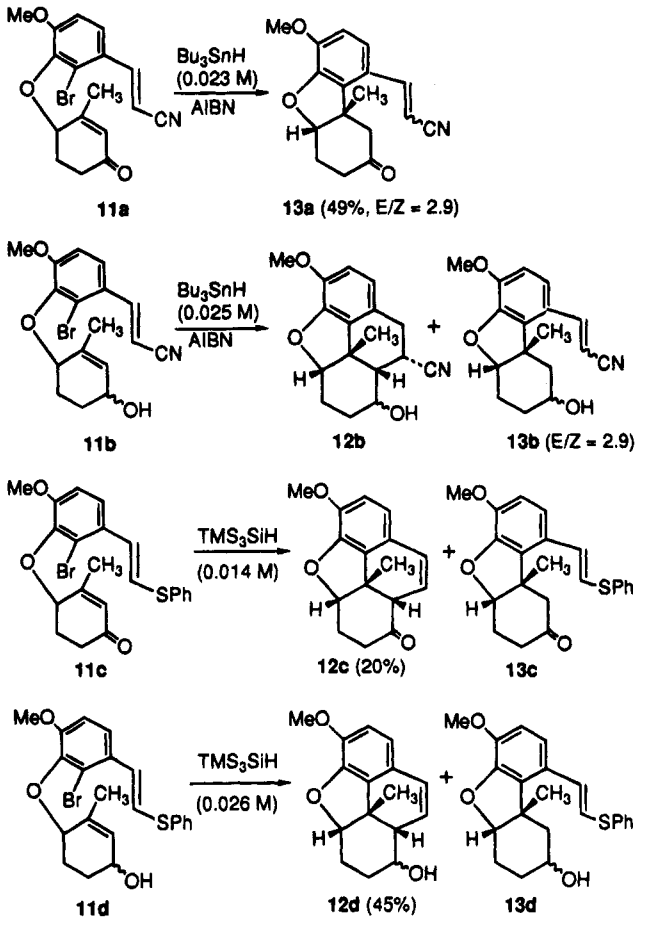
Scheme 3. Cyclization of Substrates Derived from Iodocyclohexenone 9



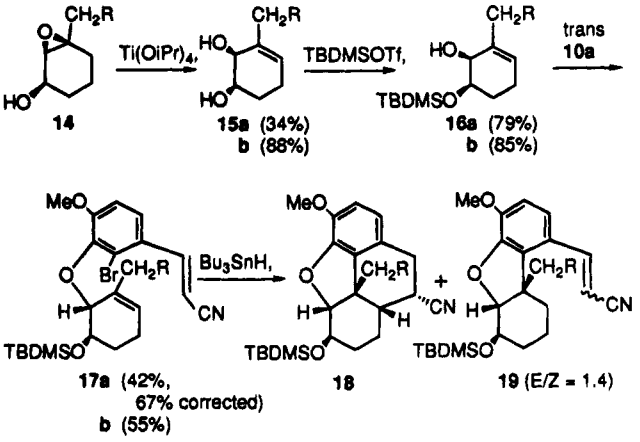
functional group pattern. In order to test this premise, γ-(aryloxy) enone **11a** was prepared by alkylation of phenol **10a**[8] with iodo ketone **9.** This alkylation proceeded in good yield. The model substrates (*Z*)- and (*E*)-**11a** were separated, and (*E*)-**11a** was subjected to radical-initiating conditions (Scheme 3).

Treatment of enone (*E*)-**11a** with tributyltin hydride (0.023 M) gave tricyclic product **13a** (49% yield) in which a single closure had taken place. Because substrates **2a** and **2b** had both undergone tandem closure under similar conditions, we attributed the absence of the second cyclization event in this reaction to the relative stability of the α-keto tricyclic radical derived from **11a**. Eventual trapping by hydride in a bimolecular event gives the observed product.

In order to remove the effect of the carbonyl group on the outcome of the cyclization, we prepared the alcohol (*E*)-**11b** by subjecting ketone (*E*)-**11a** to Luche reduction.[9] A preliminary investigation of the cyclization of substrate (*E*)-**11b** (0.025 M Bu_3SnH) revealed the presence of both tetracyclic and tricyclic products **12b** and **13b** (in an approximate ratio of 1:1 as analyzed by NMR) along with a small amount of starting material.

In order to find a system and conditions which would afford high conversion to an appropriately functionalized tetracyclic product, we decided to examine the closure of substrate **11d** with tris(trimethylsilyl)silane.[4] Preparation of **11d** required alkylation of phenol **10b** (produced as the *E* isomer only, see Experimental Section) with iodo ketone **9** and subsequent reduction of ketone **11c**. Thus, both ethers **11c** and **11d** would be available for study. Indeed, alkylation of phenol **10b** with iodo ketone **9** gave substrate **11c**, and Luche reduction of this ketone afforded the desired alcohol **11d**.

Scheme 4. Synthesis and Cyclization of Substrates Derived from Protected Diol 16



Treatment of enone **11c** with TMS_3SiH gave a modest yield of **12c** and a second fraction which appeared to be tricyclic **13c**, contaminated with small amounts of other materials. Treatment of allylic alcohol **11d** under similar conditions gave tetracyclic **12d** with a somewhat better conversion. A second fraction from this reaction mixture appeared to be largely tricyclic **13d**, contaminated with a small amount of the β-epimer of tetracyclic alcohol **12d**.

In light of the inefficiency of the tandem processes in the cyclizations of substrates of general structure **11**, the prospects of the 4-halocyclohexenone-derived substrates appeared unpromising. In addition, the tetracyclic products **12** would require carbonyl transposition for elaboration to the morphine functional group pattern. Therefore, we decided to examine a different class of intermediates.

We turned to the possibility that derivatives of diols of general structure **15** might prove accessible and useful. We imagined that the simple model diol **15a** might be obtained by regiospecific isomerization of the known epoxy cyclohexanol **14a** (Scheme 4). The Sharpless titanium isopropoxide protocol, not previously employed in cyclic systems, seemed ideal for the desired transformation. This method converts epoxy alcohols to allylic diols by removal of a proton from the carbon situated *syn* to the hydroxyalkyl substituent.[10]

Indeed, treatment of epoxy alcohol **14a**[11] with titanium isopropoxide affords cyclohexenediol **15a**, contaminated by only a trace of the exocyclic olefinic isomer, in modest yield.[12] Protection of the less hindered hydroxyl group of diol **15a** with TBDMSOTf gave alcohol **16a**. Mitsunobu coupling with the *E* isomer of phenol **10a** then gave the cyclization substrate **17a**.

Treatment of **17a** with tributyltin hydride under the standard conditions afforded a mixture of the desired tetracyclic **18a** and the tricyclic byproduct **19a** (30% yield

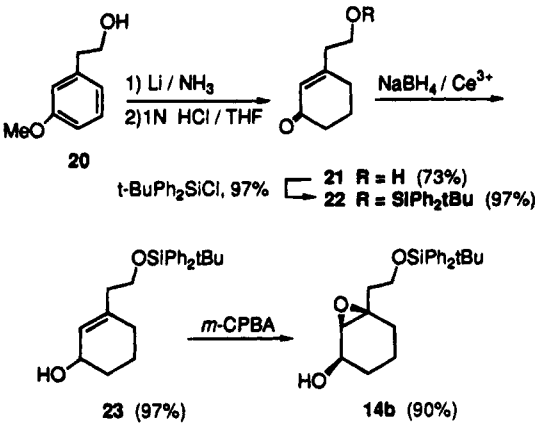
(8) Phenol **10a** was prepared by application of the Emmons–Wadsworth methodology to bromoisovanillin. The resulting cis/trans mixture was used in the alkylation shown in Scheme 2, and the resulting isomers of aryloxy enone **11a** were separated by chromatography. Only trans **11a** was used in Scheme 3. See the Experimental Section for details.

(9) Gemal, A. L.; Luche, J.-L. *J. Am. Chem. Soc.* **1981**, *103*, 5454.

(10) Morgans, D. J.; Sharpless, K. B.; Traynor, S. G. *J. Am. Chem. Soc.* **1983**, *103*, 462.

(11) Magnusson, G.; Thorén, S. *J. Org. Chem.* **1973**, *38*, 1380.

Scheme 5. Preparation of Epoxide 14b



of the mixture), not cleanly separable by chromatography, in a ratio of 2:1. Although conversion to tetracyclic material was not complete, the oxidation pattern in the model tetracycle obtained here was closer to that required for morphine synthesis than that supplied by earlier model cyclizations. Therefore, we decided to prepare a cyclization substrate which might provide not only a suitable functional group array but the entire morphine carbon skeleton.

The key epoxy alcohol **14b** was prepared in excellent yield (Scheme 5) from the inexpensive *m*-methoxyphenylacetic acid via the known alcohol **20** and enone **21**.[13] The hydroxyl group of **21** was protected as the *tert*-butyldiphenylsilyl ether, a group which we expected to tolerate the titanium isopropoxide isomerization conditions. Luche reduction of ketone **22** afforded alcohol **23** which was converted to the *Z* epoxide with *m*-chloroperoxybenzoic acid.

Titianium isopropoxide converted epoxy alcohol **14b** to enediol **15b** in excellent yield. Protection of the less hindered hydroxyl group of **15b** was also efficiently achieved. The highly and appropriately functionalized C-ring equivalent **16b** was therefore available for elaboration into a cyclization substrate.

Mitsunobu coupling of cyclohexenol **16b** with the E isomer of phenolic cinnamonitrile **10a** provided substrate **17b** (Scheme 4). Attempts to cyclize **17b** afforded a mixture which contained traces of the desired tetracyclic **18b**.

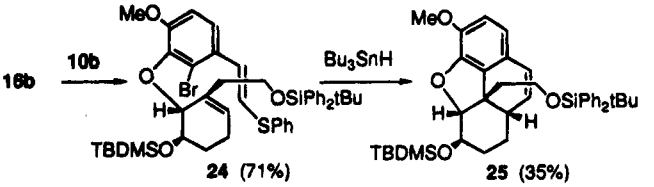
However, treatment of cyclization substrate **24** (Scheme 6), prepared by Mitsunobu coupling of **16b** and phenolic cinnamonitrile **10b** with tributyltin hydride under the standard conditions, gave tetracyclic styrene **25** in 35% yield.

Conclusions

Of the two types of styrenes examined as terminators of the radical cyclization, the phenylthio derivative appears to be a more efficient trap. Furthermore, of the two model ring-III equivalents, **9** and **16**, the latter appears the more promising.

These studies demonstrate that a functionalized two-carbon chain at C-13 does not interfere in a significant way in the outcome of the tandem closure. This result is critical to the application of the radical cyclization strategy, as developed so far, and to the total synthesis of the morphine alkaloids. Taking note of these results, we committed further efforts on this project to the preparation of a cyclization substrate which might be elaborated to dihydrocodeinone. This work is reported elsewhere.[2]

Scheme 6. Cyclization of Heavily Functionalized Substrate 24



Experimental Section

General. Melting points are uncorrected. High-resolution mass spectra were obtained under electron impact (EI), chemical ionization (CI), or fast atom bombardment (FAB) conditions. Thin layer chromatography (TLC) was carried out on precoated silica gel 60F 254 plates. Prep Plate chromatography was performed on precoated silica gel 1000-μm plates. Flash column chromatography was performed with silica gel 60 (230–400 mesh). THF and Et_2O were distilled from sodium benzophenone ketyl. Benzene was distilled from CaH_2.

4-Iodo-3-methyl-2-cyclohexen-1-one (9). To a stirred solution of LDA (14.96 mmol) at −78 °C was added 1.54 g (14 mmol) of the 3-methyl-3-cyclohexen-1-one in THF (5 mL) dropwise under argon. After the solution was stirred at −78 °C for 30 min, 3.55 g (14 mmol) of I_2 in THF (7 mL) was added dropwise. The reaction mixture was stirred at −78 °C for 5 min after the end of the addition, quenched with aqueous $NaHCO_3$, and extracted with Et_2O (3 × 50 mL). The combined organic layer was washed with 5% $Na_2S_2O_3$ and brine, dried over Na_2SO_4, filtered, and concentrated to yield 2.20 g (67%) of a brown oil which was stored in the freezer: IR ($CHCl_3$) 1667, 1620, 1467, 1431, 1378 cm^{-1}; 250-MHz ^1H NMR ($CDCl_3$) δ 5.90 (s, 1 H), 4.95 (t, 1 H, $J \approx 3$ Hz), 2.60–2.30 (m, 4 H), 2.15 (s, 3 H); HRMS (EI) for C_7H_9OI (M^+) calcd 235.9697, found 235.9683.

Phenol 10a, Z and E Isomers. To a suspension of NaH (64 mg, 2.67 mmol) in 15 mL of THF was added 0.43 mL (2.67 mmol) of diethyl (cyanomethyl)phosphonate at rt under argon, and a clear solution was formed. After the solution was stirred at rt for 20 min, 306 mg (1.32 mmol) of bromoisovanillin[14] in THF (2 mL) was added. The reaction mixture was stirred at rt for 3 h, quenched with water, and then extracted with EtOAc (2 × 30 mL). The aqueous phase was washed with EtOAc (2 × 30 mL), and the combined organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated to give the crude product. Flash chromatography on silica gel with EtOAc–Hex (1:1) yielded 206 mg (61%) of the *E*-unsaturated nitrile and 82 mg (24%) of the *Z*-isomer. For the *E*-isomer: white solid, mp 202–203 °C; IR (KBr) 3340, 2126, 1613, 1595, 1030 cm^{-1}; 250-MHz ^1H NMR ($CDCl_3$) δ 7.76 (d, 1 H, J = 16.5 Hz), 7.12 (d, 1 H, J = 8.5 Hz), 6.85 (d, 1 H, J = 8.6 Hz), 6.05 (s, 1 H), 5.75 (d, 1 H, J = 16.6 Hz), 3.95 (s, 3 H); 100.6-MHz ^{13}C NMR ($CDCl_3$ and DMSO) δ 149.49, 148.86, 143.92, 126.19, 117.87, 117.66, 111.62, 109.60, 95.81, 55.97; HRMS (EI) for $C_{10}H_8O_2{}^{79}BrN$ (M^+) calcd 252.9737, found

(12) In contrast to the titanium isopropoxide conditions, Yamamoto's reagent, diethylaluminum 2,2,6,6-tetramethylpiperidide, effected the clean conversion of **14a** to **i** in 60% yield. See: Tanaka, S; Yasuda, A.; Yamamoto, H.; Nozaki, H. *J. Am.Chem. Soc.* **1975**, *97*, 3252.

(13) Majetich, G.; Defauw, J.; Ringold, C. *J. Org. Chem.* **1988**, *53*, 50.

(14) Brotherton, R. J.; Hazlet, S. E. J. *Org. Chem.* **1962**, *27*, 3253.

252.9754. For the *Z*-isomer: off-white solid, mp 122–124 °C; 400-MHz ^{1}H NMR ($CDCl_3$) δ 7.68 (d, 1 H, J = 8.6 Hz), 7.48 (d, 1 H, J = 12.0 Hz), 6.90 (d, 1 H, J = 8.6 Hz), 6.12 (br s, 1 H), 5.49 (d, 1 H, J = 12.0 Hz), 3.95 (s, 3 H); 100.6-MHz ^{13}C NMR ($CDCl_3$) δ 148.65, 147.51, 143.50, 126.72, 120.81, 117.08, 110.78, 109.42, 96.10, 56.46.

Phenol 10b. To a stirred solution of 3.75 g (14.4 mmol) of diethyl [(phenylthio)methyl]phosphonate in 80 mL of THF at 0 °C was added 9.0 mL (16.2 mmol) of n-BuLi (1.8 M in cyclohexane) dropwise under argon. After the solution was stirred at 0 °C for 30 min, 2.0 g (8.7 mmol) of bromoisovanillin in THF (50 mL) was added to the above solution. The reaction mixture was allowed to warm to rt and then refluxed overnight. Water was then added, and the resulting mixture was extracted with CH_2Cl_2. The aqueous layer was washed with CH_2Cl_2 (3 × 70 mL), and the combined organic solution was washed with brine, dried over Na_2SO_4, and concentrated to give the crude product. Purification by flash chromatography with EtOAc–Hex–acetone (1:4:1) afforded 2.40 g (82%) of the vinyl sulfide as a white solid: mp 115.5–116 °C; IR (CH_2Cl_2) 3498, 1600, 1580, 1436, 1026 cm^{-1}; 250-MHz ^{1}H NMR ($CDCl_3$) δ 7.45–7.29 (m, 5 H), 7.04 (d, 1 H, J = 8.5 Hz), 7.01 (d, 1 H, J = 15.3 Hz), 6.79 (d, 1 H, J = 8.8 Hz), 6.74 (d, 1 H, J = 15.4 Hz), 5.95 (s, 1 H), 3.91 (s, 3 H); 100.6-MHz ^{13}C NMR ($CDCl_3$) δ 146.4, 143.2, 135.1, 130.2, 130.0, 129.9, 129.2, 127.1, 124.9, 117.6, 109.8, 109.7, 56.4; HRMS (EI) for $C_{15}H_{13}O_2{}^{79}BrS$ (M^+) calcd 335.9819, found 335.9804.

(Aryloxy)cyclohexenones (*Z*)- and (*E*)-11a and -11c. To a stirred solution of n-Bu_4NF (2 equiv) and 1 equiv of the phenolic substrate (**10a** or **10b**) in 5 mL of DMF at rt was added 1 equiv of the iodo enone **9** as a DMF solution. The reaction mixture was stirred at rt overnight, and then water was added and the resulting mixture extracted with EtOAc (3×). The organic phase was washed several times with brine, dried over Na_2SO_4, filtered, and concentrated to give the crude product. Purification by flash chromatography on silica gel yielded the desired (aryloxy)cyclohexenone ethers.

11a: yellow oil, 73% yield (EtOAc–Hex (1:2)). For the *Z*-isomer: IR (CH_2Cl_2) 3048, 2213, 1668, 1609, 1582, 1031 cm^{-1}; 400-MHz ^{1}H NMR ($CDCl_3$) δ 7.88 (d, 1 H, J = 8.8 Hz), 7.47 (d, 1 H, J = 12.0 Hz), 7.01 (d, 1 H, J = 8.8 Hz), 5.95 (s, 1 H), 5.50 (d, 1 H, J = 11.9 Hz), 5.08 (d, 1 H, J = 6.2 Hz), 3.92 (s, 3 H), 2.80 (m, 1 H), 2.28 (m, 2 H), 2.19 (s, 3 H), 2.05 (m, 1 H); 100.6-MHz ^{13}C NMR ($CDCl_3$) δ 198.1, 159.2, 154.5, 147.3, 143.5, 127.9, 126.7, 124.7, 120.6, 116.6, 110.9, 96.1, 77.4, 55.8, 34.0, 28.0, 21.1; HRMS (EI) for $C_{17}H_{16}O_3NBr$ ($M^+ - C_7H_8O$) calcd 252.9738, found 252.9751. For the *E*-isomer: IR (CH_2Cl_2) 3048, 2213, 1668, 1609, 1582, 1025 cm^{-1}; 400-MHz ^{1}H NMR ($CDCl_3$) δ 7.78 (d, 1 H, J = 16.6 Hz), 7.33 (d, 1 H, J = 8.7 Hz), 6.93 (d, 1 H, J = 8.7 Hz), 5.98 (s, 1 H), 5.75 (d, 1 H, J = 16.6 Hz), 5.07 (d, 1 H, J = 6.5 Hz), 3.92 (s, 3 H), 2.80 (m, 1 H), 2.28 (m, 2 H), 2.19 (s, 3 H), 2.05 (m, 1 H); 100.6-MHz ^{13}C NMR ($CDCl_3$) δ 198.4, 159.4, 155.2, 148.9, 144.0, 128.3, 127.3, 122.7, 121.3, 117.9, 111.4, 97.1, 77.8, 56.1, 34.4, 28.4, 21.3.

11c: orange oil, 55% yield (EtOAc–Hex (1:2)); IR (CH_2Cl_2) 3045, 1667, 1624, 1581, 1028 cm^{-1}; 250-MHz ^{1}H NMR ($CDCl_3$) δ 7.48–7.20 (m, 6 H), 7.02 (d, 1 H, J = 15.3 Hz), 6.87 (d, 1 H, J = 8.8 Hz), 6.73 (d, 1 H, J = 15.2 Hz), 5.95 (s, 1 H), 5.03 (s, 1 H), 3.87 (s, 3 H), 2.80 (m, 1 H), 2.35–2.15 (m, 5 H), 2.05 (m, 1 H).; HRMS (EI) for $C_{22}H_{21}O_3{}^{79}BrS$ (M^+) calcd 444.0394, found 444.0368.

Cyclohexenols 11b and 11d. To a solution of enone **11a** or **11c** (1 equiv) and $CeCl_3{\cdot}7H_2O$ (1 equiv) in MeOH at rt was added a slight excess of $NaBH_4$ in small portions. After the solution was stirred at rt for 1 h, water was added to destroy excess hydride, and the resulting mixture was extracted with CH_2Cl_2. The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated to give the alcohol without any further purification.

11b: isolated in 71–85% yield. For the *E*-isomer: off-white solid, mp 139–140 °C; IR (CH_2Cl_2) 3505, 3055, 2209, 1607, 1580, 1029 cm^{-1}; 400-MHz ^{1}H NMR ($CDCl_3$) δ 7.82 (d, 1 H, J = 16.5 Hz), 7.30 (d, 1 H, J = 8.8 Hz), 6.90 (d, 1 H, J = 8.7 Hz), 5.75 (d, 1 H, J = 16.5 Hz), 5.72 (s , 1 H), 4.82 (t, 0.2 H, J = 4.7 Hz), 4.68 (t, 0.8 H, J = 3.9 Hz), 4.30 (br s, 0.2 H), 4.15 (br s, 0.8 H), 3.90 (s, 3 H), 2.35–1.78 (m, 8 H); 100.6-MHz ^{13}C (for one epimer) NMR ($CDCl_3$) δ 155.49, 149.38, 145.08, 136.23, 130.78, 127.26, 122.18, 121.52, 118.07, 111.31, 96.70, 77.98, 67.05, 55.92, 28.27, 25.63, 20.70; HRMS (EI) for $C_{17}H_{18}O_3N$-^{79}Br ($M^+ - C_7H_{10}O$) calcd 252.9738, found 252.9758. For the *Z*-isomer: pale yellow oil; IR ($CHCl_3$) 3460, 3052, 2217, 1606, 1584, 1033 cm^{-1}; 400-MHz ^{1}H NMR ($CDCl_3$) δ 7.85 (d, 1 H, J = 8.8 Hz), 7.50 (d, 1 H, J = 12.0 Hz), 6.95 (d, 1 H, J = 8.7 Hz), 5.75 (s, 1 H), 5.48 (d, 1 H , J = 12.0 Hz), 4.82 (t, 0.2 H, J = 4.8 Hz), 4.68 (t, 0.8 H, J = 3.7 Hz), 4.30 (br s, 0.2 H), 4.15 (br s, 0.8 H), 3.90 (s, 3 H), 2.05–1.82 (m, 6 H), 1.65–1.45 (m, 2 H).

11d: yellow oil, 85% yield; IR (CH_2Cl_2) 3443, 1667, 1581, 1028 cm^{-1}; 400-MHz ^{1}H NMR ($CDCl_3$) δ 7.45 (d, 2 H, J = 7.4 Hz), 7.35 (t, 2 H, J = 7.3 Hz), 7.25 (t, 1 H, J = 7.1 Hz), 7.20 (d, 1 H, J = 8.6 Hz), 7.05 (d, 1 H, J = 15.3 Hz), 6.83 (d, 1 H, J = 8.7 Hz), 6.72 (d, 1 H, J = 15.3 Hz), 5.72 (s, 1 H), 4.78 (t, 0.2 H, J = 4.9 Hz), 4.68 (t, 0.8 H, J = 3.8 Hz), 4.29 (br s, 0.2 H), 4.13 (br s, 0.8 H), 3.85 (s, 3 H), 2.15–1.45 (m, 8 H); HRMS (EI) for $C_{22}H_{23}O_3{}^{79}BrS$ (M^+) calcd 446.0550, found 446.0528.

General Procedure for the Bu_3SnH or TMS_3SiH Radical Cyclizations. A solution of 1 equiv of the substrate, 1.2–1.5 equiv of tributyltin hydride or TMS_3SiH, and a catalytic amount of AIBN (0.1 equiv) in 3–5 mL of dry benzene was heated in a degassed sealed tube at 120–130 °C for 24–48 h. The reaction was monitored by TLC, and after the complete consumption of the starting material the solvent was evaporated and the resulting residue was dissolved in Et_2O. The ethereal solution was washed several times with 10% KF[15] (only when Bu_3SnH was used) and brine, dried over Na_2SO_4, filtered, and concentrated to give the crude product. Purification of the crude product by flash chromatography or preparative TLC over silica gel yielded the desired products.

Tricyclic ketone 13a: yellow oil, 49% yield (preparative TLC in EtOAc–Hex (1:1)). For the *E*-isomer: IR (CH_2Cl_2) 3055, 1713, 1602, 1575, 1507, 1047, 1026 cm^{-1}; 250-MHz ^{1}H NMR ($CDCl_3$) δ 7.52 (d, 1 H, J = 16.6 Hz), 7.05 (d, 1 H, J = 8.6 Hz), 6.78 (d, 1 H, J = 8.5 Hz), 5.72 (d, 1 H, J = 16.3 Hz), 4.71 (s, 1 H), 3.90 (s, 3 H), 2.70 (dd, 2 H, J = 15.1, 14.9 Hz), 2.35 (m, 2 H), 1.70 (m, 2 H), 1.55 (s, 3 H); HRMS (EI) for $C_{17}H_{17}O_3N$ (M^+) calcd 283.1208, found 283.1222.

Tricyclic ketone 12c: yellow oil, 20% yield (preparative TLC in EtOAc–Hex–acetone (1:5:1)); 250-MHz ^{1}H NMR ($CDCl_3$) δ 6.68 (ABq, 2 H, J = 8.0 Hz), 6.58 (dd, 1 H, J = 9.6, 1.3 Hz), 5.98 (dd, 1 H, J = 6.2, 9.5 Hz), 4.95 (t, 1 H, $J \approx$ 6.3 Hz), 3.90 (s, 3 H), 3.05 (d, 1 H, J = 6.1 Hz), 2.42–2.10 (m, 3 H), 2.00 (m, 1 H), 1.41 (s, 3 H).

Tetracyclic alcohol 12d: yellow oil, 45% yield of a mixture of epimers (preparative TLC in EtOAc–Hex (1:2)). A second preparative TLC resulted in isolation of the α-epimer: IR (CH_2Cl_2) 3527, 3055, 1607, 1499, 1053, 1027 cm^{-1}; 250-MHz ^{1}H NMR ($CDCl_3$) δ 6.78 (dd, 1 H, J = 9.6, 1.1 Hz), 6.65 (s, 2 H), 5.72 (dd, 1 H, J = 9.6, 5.8 Hz), 4.70 (dd, 1 H , J = 9.8, 6.8 Hz), 3.85 (s, 4 H), 2.50 (t, 1 H, $J \approx$ 4.9 Hz), 1.85 (m, 3 H), 1.70 (s, 1 H), 1.33 (m, 1 H), 1.20 (s, 3 H); 100.6-MHz ^{13}C NMR ($CDCl_3$) δ 145.60, 143.19, 132.58, 128.17, 124.82, 122.65, 117.69, 111.98, 91.84, 65.29, 56.14, 46.64, 39.40, 26.76, 25.92, 21.19; HRMS (EI) for $C_{16}H_{18}O_3$ (M^+) calcd 258.1255, found 258.1260.

Diol 15a. A solution of 1.06 g (8.28 mmol) of the epoxy alcohol **14a** and 2.95 mL (9.93 mmol) of $Ti(OiPr)_4$ (distilled from CaH_2) in 20 mL of CH_2Cl_2 was stirred at rt overnight. The solvent was evaporated and the resulting yellow residue dissolved in Et_2O (50 mL) and treated with 5% HCl in an ice bath under stirring. The initial white heavy precipitate was gradually dissolved, leaving two clear layers. After the ethereal phase was separated, the aqueous phase was extracted several times with EtOAc (5 × 50 mL). The combined organic phase was dried over Na_2SO_4, filtered, and concentrated to give the crude product. Flash chromatography over silica gel with EtOAc–acetone–Hex (1:2:1) yielded 363 mg (34%) of the diol as a colorless oil: IR (CH_2Cl_2) 3392 (br), 3050, 1617, 1446, 1073, 1036 cm^{-1}; 400-MHz ^{1}H NMR ($CDCl_3$) δ 5.55 (m, 1 H), 3.92 (d, 1 H, J = 3.8 Hz), 3.74 (m, 1 H), 2.55 (br s, 1 H), 2.40 (br s, 1 H), 2.15–1.95 (m, 2 H), 1.80 (d, 3 H, J = 1.7 Hz), 1.68 (m, 2 H); HRMS (EI) for $C_7H_{12}O_2$ (M^+) calcd 128.0834, found 128.0837.

(15) Jacobs, J.; Leibner, J. E. J. *Org. Chem.* **1979**, *44*, 449.

Alcohol 16a. A solution of 67 mg (0.53 mmol) of the diol **15a**, 183 μL (0.13 mmol) of NEt_3, and 182 μL (0.80 mmol) of TBDMSOTf in 5 mL of CH_2Cl_2 was stirred at rt for 5 h. The reaction mixture was then quenched with water, the organic layer was separated, and the remaining aqueous phase was extracted with CH_2Cl_2 (2 × 30 mL). The combined organic layer was washed with 5% HCl, H_2O, and brine, dried over Na_2SO_4, filtered, and concentrated to give an oily residue. Purification by flash chromatography on silica gel with EtOAc–Hex (1:9) yielded 102 mg (79%) of the protected alcohol as a colorless oil: IR (neat) 3558, 3483 (br), 3027, 1462, 1372, 1250, 1085, 1037 cm^{-1}; 250-MHz ^{1}H NMR ($CDCl_3$) δ, 5.55 (s, 1 H), 3.82 (d, 1 H, J = 2.3 Hz), 3.75 (q, 1 H), 2.69 (d, 1 H, J = 2.2 Hz), 2.18 - 1.90 (m, 2 H), 1.82 (d, 3 H, J = 1.8 Hz), 1.70 (m, 1 H), 1.55 (m, 1 H), 0.92 (s, 9 H), 0.10 (s, 6 H); HRMS (EI) for $C_{13}H_{26}O_2Si$ (M^+ − OH) calcd 225.1674, found 225.1658.

Aryl Ether 17a. To a solution of 37 mg (0.152 mmol) of alcohol **16a** and 76 μL (0.304 mmol) of PBu_3 in 5 mL of THF at −25 °C (dry ice–CCl_4) was added 10 μL (0.064 mmol) of neat DEAD under argon, and the orange color of the diester faded rapidly. Stirring at −25 °C was continued for 10 min, after which time exactly one fifth of a solution of the E isomer of phenol **10a** (38 mg, 0.150 mmol) in 1 mL of THF was added dropwise. The resulting mixture was stirred at −25 °C for 1 h. The same sequential additions of DEAD [10 μL/10 min at −25 °C/one fifth of phenol solution/1 h at −25 °C] were repeated four more times until a total of 53 mg (0.304 mmol) of DEAD had been used and all of the phenol solution had been added. The reaction mixture was then allowed to warm to rt gradually after the last addition of phenol solution. The solvent was evaporated, and the crude aryl ether was purified by flash chromatography over silica gel with EtOAc–Hex (1:4) to yield 30 mg (42%) of the aryl ether as a white solid and 14 mg of recovered alcohol **16a** (corrected yield of **17a**, 67%), mp 139.5–140.5 °C: IR (CH_2Cl_2) 3042, 2210, 1614, 1577, 1478, 1080, 1031 cm^{-1}; 250-MHz ^{1}H NMR ($CDCl_3$) δ 7.83 (d, 1 H, J = 16.2 Hz), 7.30 (d, 1 H, J = 8.9 Hz), 6.90 (d, 1 H, J = 8.7 Hz), 5.78 (s, 1 H), 5.72 (d, 1 H, J = 16.5 Hz), 4.45 (s, 1 H), 3.97 (q, 1 H), 3.90 (s, 3 H), 2.25–1.90 (m, 3 H), 1.87 (s, 3 H), 1.68 (m, 1 H), 0.75 (s, 9 H), −0.15 (s, 3 H), −0.20 (s, 3 H); 100.6-MHz ^{13}C NMR ($CDCl_3$) δ 155.14, 149.44, 145.50, 129.62, 128.24, 127.15, 121.95, 121.25, 118.11, 111.28, 96.61, 81.65, 67.93, 55.82, 25.64, 25.40, 21.67, 20.72, 18.04, −4.93, −5.18; HRMS (EI) for $C_{23}H_{32}O_3{}^{79}BrSiN$ (M^+ − $C_{13}H_{24}OSi$) calcd 252.9737, found 252.9732.

Tetracyclic Nitrile 18a and Tricyclic Nitrile 19a. A solution of 24.2 mg (0.051 mmol) of aryl ether **17a**, a small amount of AIBN (0.1 equiv), and 19 μL of Bu_3SnH in 4.5 mL of benzene was heated in a sealed tube at 120 °C for 32 h. After the solvent was evaporated, the resulting residue was dissolved in Et_2O and washed several times with 10% KF. The ethereal solution was washed with H_2O, dried over Na_2SO_4, and concentrated to give the crude product. Purification by flash chromatography on silica gel with EtOAc–Hex (1:6) yielded 6.1 mg (30%) of a mixture of the tetracyclic nitrile **18a** and tricyclic nitrile **19a** in a 2:1 ratio. The 400-MHz ^{1}H NMR spectrum ($CDCl_3$) of this mixture exhibited the following peaks which were attributed to **18a**: δ 6.75 (d, 1 H, J = 8.3 Hz), 6.60 (d, 1 H, J = 8.3 Hz), 4.30 (d, 1 H, J = 7.0 Hz), 3.87 (s, 3 H), 3.38 (m, 1 H), 3.22 (m, 1 H), 3.10 (dd, 1 H, J = 6.8, 17.0 Hz), 2.78 (dd, 1 H, J = 12.2, 17.1 Hz), 2.20 (m, 1 H), 2.10–1.65 (m, 4 H), 1.35 (s, 3 H), 0.9 (s, 9 H), 0.0 (s, 6 H). In addition, the following peaks which we believe to be characteristic of tricyclic **19a** were observed: 5.61 (d, J = 16.5 Hz, 0.6 H, (*E*)-styrene proton), 5.22 (d, J = 12.1 Hz, 0.4 H, (*Z*)-styrene proton), 4.25 (s, 1 H adjacent to the ether oxygen), 3.93 (3H, OMe), and 1.25 (s, 3H, angular methyl).

Alcohol 20. To a solution of 10.0 g (60 mmol) of 3-methoxyphenylacetic acid in 100 mL of THF at 0 °C was added 78 mL (78 mmol) of 1.0 M BH_3·THF dropwise. After the solution was stirred at rt for 2 h, water was added to destroy the excess of borane followed by addition of solid K_2CO_3. After the organic phase was separated, the aqueous layer was extracted with Et_2O (3 × 70 mL). The combined organic layer was washed with aqueous NaCl, dried over Na_2SO_4, filtered, and concentrated to give a colorless liquid. Kugelrohr distillation (125 °C, 8 mmHg) afforded 8.85 g (97%) of the alcohol as a colorless oil: IR (neat) 3564–3146 (br), 3046, 1597, 1040 cm^{-1}; 250-MHz ^{1}H NMR ($CDCl_3$) δ, 7.21 (m, 1 H), 6.78 (m, 3 H), 3.85 (t, 2 H, J = 6.6 Hz), 3.76 (s, 3 H), 2.82 (t, 2 H, J = 6.5 Hz), 1.78 (br s, 1 H).

Enone 21. Anhydrous NH_3 (100 mL) was distilled to a solution of 7.5 g (49.3 mmol) of alcohol **20** and 9.3 mL (98.6 mmol) of t-BuOH in 100 mL THF at −78 °C. Then, 1.4 g (202 mmol) of lithium metal was added in small portions until the blue color became persistent. After the solution was stirred at −78 °C for 4 h, a MeOH–aqueous NH_4Cl solution was added to discharge the blue color. The ammonia was evaporated, and the resulting solution was acidified with concentrated HCl until pH = 1 and then stirred at rt for 24 h. After it was saturated with solid NaCl, the organic phase was separated and the remaining aqueous layer was washed several times with EtOAc (6 × 80 mL). The combined organic phase was washed with brine, dried over Na_2SO_4, and concentrated to give the crude product. Flash chromatography on silica gel with EtOAc–Hex–acetone (1:2:1) yielded 5.02 g (73%) of the enone as a yellow oil: IR (neat) 3434, 3035, 1656, 1622, 1046 cm^{-1}; 250-MHz ^{1}H NMR ($CDCl_3$) δ 5.92 (s, 1 H), 3.83 (t, 2 H, J = 6.3 Hz), 2.50 (t, 3 H, J = 6.3 Hz), 2.35 (q, 5 H), 2.01 (quintet, 2 H); 100.6-MHz ^{13}C NMR ($CDCl_3$) δ 199.84, 163.13, 127.02, 59.95, 40.88, 37.19, 29.76, 22.55; HRMS (EI) for $C_8H_{12}O_2$ (M^+) calcd 140.0837, found 140.0813.

Silyl Ether 22. To a solution of 380 mg (2.71 mmol) of hydroxy enone **21**, 0.44 mL (3.16 mmol) of NEt_3, and 127 mg (1.04 mmol) of *N,N*-dimethyl-4-aminopyridine (DMAP) in 10 mL of CH_2Cl_2 was added 0.82 mL (3.15 mmol) of *tert*-butyldiphenylsilyl chloride. After being stirred at rt overnight, the reaction mixture was washed with aqueous HCl and aqueous NaCl, dried over Na_2SO_4, and concentrated to give the crude product. Purification by flash chromatography over silica gel with EtOAc–Hex (1:4) afforded 970 mg (97%) of the silyl ether as a yellow oil: IR ($CDCl_3$) 3061, 1667, 1626, 1590, 1467, 1097, 1050 cm^{-1}; 400-MHz ^{1}H NMR ($CDCl_3$) δ 7.65 (m, 4 H), 7.40 (m, 6 H), 5.90 (s, 1 H), 3.82 (t, 2 H, J = 6.4 Hz), 2.43 (t, 2 H, J = 6.2 Hz), 2.33 (t, 2 H, J = 6.3 Hz), 2.25 (t, 2 H, J = 6.3 Hz), 1.95 (m, 2 H), 1.05 (s, 9 H); 100.6-MHz ^{13}C NMR ($CDCl_3$) δ 199.61, 163.52, 135.48, 133.38, 129.72, 127.68, 127.29, 61.65, 40.93, 37.22, 29.78, 26.75, 22.58, 19.09; HRMS (EI) for $C_{24}H_{30}O_2Si$ (M^+ − $C(CH_3)_3$) calcd 321.1305, found 321.1304.

Allylic Alcohol 23. To a solution of 950 mg (2.51 mmol) of enone **22** and 935 mg (2.51 mmol) of $CeCl_3$·$7H_2O$ in 10 mL of MeOH was added 95 mg (2.51 mmol) of $NaBH_4$. After the solution was stirred at rt for 30 min, water was added to quench the hydride excess, and the resulting mixture was extracted with CH_2Cl_2 (4 × 40 mL). The combined organic layer was washed with aqueous NaCl, dried over Na_2SO_4, filtered, and concentrated to give 928 mg (97%) of the alcohol as a colorless oil: IR ($CDCl_3$) 3589, 3425 (br), 3060, 3037, 1661, 1584, 1467, 1037 cm^{-1}; 400-MHz ^{1}H NMR ($CDCl_3$) δ 7.65 (m, 4 H), 7.38 (m, 6 H), 5.50 (d, 1 H, J = 1.6 Hz), 4.12 (s, 1 H), 3.73 (t, 2 H, J = 6.8 Hz), 2.22 (m, 2 H), 1.95–1.60 (m, 4 H), 1.55 (m, 2 H), 1.45 (br s, 1 H), 1.05 (s, 9 H); 100.6-MHz ^{13}C NMR ($CDCl_3$) δ, 139.41, 135.53, 133.88, 129.55, 127.58, 125.78, 65.77, 62.55, 40.56, 31.71, 28.67, 26.81, 19.16, 19.03; HRMS (EI) for $C_{24}H_{32}O_2Si$ (M^+ − $C(CH_3)_3$ − H_2O) calcd 305.1356, found 305.1386.

Epoxy Alcohol 14b. A solution of 928 mg (2.44 mmol) of allylic alcohol **23**, in 10 mL of CH_2Cl_2 at 0 °C, was treated with 725 mg (2.52 mmol) of 50–60% *m*-CPBA. After being stirred at 0 °C for 30 min, the reaction mixture was filtered and the resulting filtrate was stirred vigorously with 10% Na_2SO_3. The organic phase was next washed with aqueous $NaHCO_3$ and aqueous NaCl, dried over Na_2SO_4, filtered, and concentrated to give the crude product. Kugelrohr distillation of the volatile impurities afforded 877 mg (90%) of the epoxy alcohol as a viscous yellow oil: IR (neat) 3413 (br), 3073, 3049, 1590, 1467, 1032 cm^{-1}; 400-MHz ^{1}H NMR ($CDCl_3$) δ 7.67 (m, 4 H), 7.39 (m, 6 H), 3.98 (br s, 1 H), 3.75 (t, 2 H, J = 6.4 Hz), 3.22 (d, 1 H, J = 3.0 Hz), 2.45 (br s, 1 H), 1.90 (m, 1 H), 1.72 (m, 3 H), 1.49 (m, 3 H), 1.22 (m, 1 H), 1.05 (s, 9 H); 100.6-MHz ^{13}C NMR ($CDCl_3$) δ, 135.40, 133.41, 133.34, 129.62,

127.61, 66.70, 62.56, 61.63, 60.28, 40.12, 28.88, 26.76, 26.71, 18.99, 18.06; HRMS (EI) for $C_{24}H_{32}O_3Si$ ($M^+ - C(CH_3)_3 - H_2O$) calcd 321.1305, found 321.1288.

Diol 15b. A solution of 774 mg (1.95 mmol) of the epoxy alcohol **14b** and 0.87 mL (2.93 mmol) of $Ti(OiPr)_4$ in 20 mL of benzene was refluxed for 6 h. The solvent was evaporated, and the resulting residue was dissolved in 25 mL of Et_2O and treated with 5% HCl in an ice bath. The initially white precipitate was gradually dissolved, leaving two clear phases. After the Et_2O phase was separated, the aqueous phase was extracted with EtOAc (3 × 30 mL). The combined organic phase was washed with aqueous NaCl, dried over Na_2SO_4, and concentrated to give the crude diol. Purification by flash chromatography on silica gel with EtOAc–Hex–acetone (1:3:1) afforded 684 mg (88%) of the diol as a yellow oil: IR (CH_2Cl_2) 3559, 3415, 3046, 1589, 1467, 1077, 1041 cm^{-1}; 400-MHz ^1H NMR ($CDCl_3$) δ 7.68 (m, 4 H), 7.40 (m, 6 H), 5.58 (s, 1 H), 4.02 (d, 1 H, J = 3.5 Hz), 3.82 (m, 1 H), 3.70 (m, 3 H), 2.70 (br s, 1 H), 2.38 (m, 1 H), 2.35–2.15 (m, 2 H), 2.05 (m, 1 H), 1.73 (m, 2 H), 1.05 (s, 9 H); 100.6-MHz ^{13}C NMR ($CDCl_3$) δ 135.61, 135.59, 135.53, 133.10, 129.86, 129.83, 127.78, 127.77, 69.54, 68.81, 64.41, 37.97, 26.81, 25.54, 24.11, 19.11; HRMS (EI) for $C_{24}H_{32}O_3Si$ ($M^+ - C(CH_3)_3 - H_2O$) calcd 321.1305, found 321.1306.

Alcohol 16b. To a solution of 100 mg (0.252 mmol) of diol **15b** and 88 μL (0.504 mmol) of diisopropylethylamine in 5 mL of CH_2Cl_2 at 0 °C was added 81 μL (0.352 mmol) of TBDMSOTf. After being stirred at 0 °C for 30 min, the reaction mixture was quenched with water, and the organic phase was separated. The aqueous phase was washed with CH_2Cl_2, and the combined organic layer was washed with aqueous HCl and aqueous NaCl, dried over Na_2SO_4, and concentrated to give the crude product. Flash chromatography on silica gel with EtOAc–Hex (1:6) afforded 109 mg (85%) of the silyl ether as a colorless oil: IR (CH_2Cl_2) 3538, 3047, 1588, 1471, 1038 cm^{-1}; 400-MHz ^1H NMR ($CDCl_3$) δ 7.67 (m, 4 H), 7.40 (m, 6 H), 5.55 (s, 1 H), 3.85 (d, 1 H, J = 3.6 Hz), 3.82 - 3.70 (m, 3 H), 2.63 (br s, 1 H), 2.39 (m, 2 H), 2.15 (d, 1 H, J = 17.7 Hz), 2.0 (m, 1 H), 1.75 (m, 1 H), 1.55 (m, 1 H), 1.05 (s, 9 H), 0.88 (s, 9 H), 0.03 (s, 6 H); 100.6-MHz ^{13}C NMR ($CDCl_3$) δ, 135.57, 134.67, 134.00, 129.50, 127.57, 126.74, 71.14, 68.87, 63.08, 37.67, 26.83, 25.81, 25.33, 24.27, 19.18, 18.07, −4.45, −4.84; HRMS (EI) for $C_{30}H_{46}O_3Si_2$ ($M^+ - C(CH_3)_3$) calcd 453.2282, found 453.2309.

Aryl Ether 17b. Isolated in 55% yield, after preparation by the procedure given for ether **17a**, as a colorless oil after flash chromatography (EtOAc–Hex (1:4)): IR ($CHCl_3$) 3060, 3037, 2219, 1611, 1580, 1477, 1029 cm^{-1}; 400-MHz ^1H NMR ($CDCl_3$) δ 7.80 (d, 1 H, J = 16.5 Hz), 7.65 (m, 4 H), 7.37 (m, 6 H), 7.25 (d, 1 H, J = 8.7 Hz), 6.83 (d, 1 H, J = 8.8 Hz), 5.76 (s, 1 H), 5.70 (d, 1 H, J = 16.5 Hz), 4.48 (s, 1 H), 3.93 (s, 1 H), 3.78 (s, 5 H), 2.60 (m, 1 H), 2.42 (m, 1 H), 2.15 (m, 2 H), 2.02 (d, 1 H), 1.63 (m, 1 H), 1.05 (s, 9 H), 0.70 (s, 9 H), −0.15 (s, 3 H), −0.25 (s, 3 H); 100.6-MHz ^{13}C NMR ($CDCl_3$) δ 154.99, 149.46, 145.33, 135.56, 135.54, 134.19, 130.18, 129.44, 127.63, 127.53, 127.11, 121.86, 121.25, 118.12, 11.21, 96.58, 80.22, 67.89, 63.55, 55.66, 37.66, 26.86, 25.60, 25.42, 20.86, 19.23, 17.93, −4.97, −5.23; HRMS (FAB) for $C_{40}H_{52}O_4{}^{81}BrNSi_2$ ($M^+ - C(CH_3)_3$) calcd 690.1882, found 690.1873.

Aryl Ether 24. Isolated in 71% yield, from a procedure similar to that given for aryl ether **17b**, as a colorless oil after flash chromatography on silica gel (EtOAc–Hex (1:9)): IR (CH_2Cl_2) 3072, 3037, 1578, 1472, 1085, 1031 cm^{-1}; 400-MHz ^1H NMR ($CDCl_3$) δ 7.68 (m, 4 H), 7.45–7.25 (m, 11 H), 7.18 (d, 1 H, J = 8.7 Hz), 7.05 (d, 1 H, J = 15.4 Hz), 6.80 (d, 1 H, J = 8.7 Hz), 6.70 (d, 1 H, J = 15.3 Hz), 5.78 (d, 1 H, J = 4.9 Hz), 4.45 (s, 1 H), 3.95 (s, 1 H), 3.80 (m, 2 H), 3.73 (s, 3 H), 2.65 (m, 1 H), 2.45 (m, 1 H), 2.18 (d, 2 H, J = 8.9 Hz), 2.0 (m, 1 H), 1.62 (m, 1 H), 1.05 (s, 9 H), 0.70 (s, 9 H), −0.18 (s, 3 H), −0.25 (s, 3 H); 100.6-MHz ^{13}C NMR ($CDCl_3$) δ 152.45, 144.81, 135.56, 135.54, 135.17, 134.24, 130.66, 130.38, 130.30, 129.93, 129.87, 129.40, 129.13, 127.52, 126.96, 124.32, 121.19, 119.53, 111.19, 79.77, 67.54, 63.62, 55.54, 37.70, 26.87, 25.64, 25.23, 20.76, 19.23, 17.94, −5.06, −5.23; MS (FAB) for $C_{45}H_{57}O_4BrSSi_2$ (M^+) m/e 828.

Tetracyclic Styrene 25. A solution of 25 mg (0.030 mmol) of aryl ether **24**, 15 μL (0.056 mmol) of Bu_3SnH, and a catalytic amount of AIBN in 3.6 mL of benzene was heated in a sealed tube at 120–130 °C for 36 h. The solvent was then evaporated and the resulting residue was dissolved in Et_2O and stirred vigorously with 10% KF. The organic phase was then washed with brine, dried over Na_2SO_4, and concentrated to give the crude product. Preparative TLC on silica gel with EtOAc–Hex (1:3) gave a fraction which contained enone **22**[16] and materials containing the tributyltin moiety and a second fraction consisting of 6.7 mg (35%) of the tetracyclic compound: IR ($CDCl_3$) 3072, 1637, 1555, 1496, 1061 cm^{-1}; 250-MHz ^1H NMR ($CDCl_3$) δ 7.65 (m, 4 H), 7.40 (m, 6 H), 6.68 (d, 1 H, J = 8.0 Hz), 6.58 (d, 1 H, J = 8.0 Hz), 6.31 (d, 1 H, J = 9.5 Hz), 5.75 (dd, 1 H, J = 9.5, J = 5.8 Hz), 4.78 (d, 1 H, J = 7.0 Hz), 3.88 (s, 3 H), 3.72 (t, 2 H, J = 6.3 Hz), 3.39 (m, 1 H), 2.48 (m, 2 H), 2.30 (m, 1 H), 1.90–1.65 (m, 4 H), 1.05 (s, 9 H), 0.90 (s, 9 H), 0.05 (d, 6 H); HRMS (FAB) for $C_{39}H_{52}O_4Si_2$ ($M^+ - C(CH_3)_3$) calcd 583.2702, found 583.2745.

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Supplementary Material Available: Copies of ^1H NMR spectra of all new compounds and copies of ^{13}C NMR spectra of **10**, **11**, **12d**, **14b**, **16b**, **17b**, and **21–24** (43 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(16) A mechanism for the fragmentation of a cyclization substrate related to **24** to the corresponding enone is proposed in ref 2.